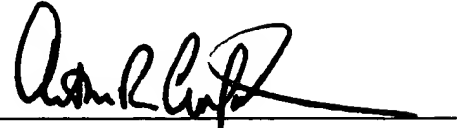


MISHRA et al
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Respectfully submitted,

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EXPLANATION OF SOURCE OF NEW CLAIMS

The following claims (claim 15, 16, 17, 18, and 19) are derived from original claim 13 .

15. [The] A method of reducing or substantially completely eliminating irritation upon injection of formulations containing propofol by administering a stable, sterile, and antimicrobial, aqueous dispersion of water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of about 1% to about 15% of propofol [as the active ingredient], up to about 7% of a propofol soluble diluent, and about 0.8% to about 4% of a surface stabilizing amphiphilic agent, and the aqueous phase comprising a pharmaceutically acceptable water-soluble polyhydroxy tonicity modifier, and the composition being devoid of additional bactericidal or bacteriostatic preservative agents, provided the ratio of propofol to diluent is about 1:4 to about 1:0.1, and the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5, and the composition has a viscosity of from about 0.8 to about 15 centipoise.
16. [The] A method of reducing or substantially completely eliminating irritation upon injection of formulations containing propofol by administering a stable, sterile, and antimicrobial, aqueous dispersion of water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of about 1% to about 15% of propofol [as the active ingredient], up to about 7% of a propofol soluble diluent, and about 0.8% to about 4% of a surface stabilizing amphiphilic agent, and the aqueous phase comprising a pharmaceutically acceptable water-soluble polyhydroxy tonicity

modifier, the composition being devoid of additional bactericidal or bacteriostatic preservative agents.

17. The method of claim 16 where the ratio of propofol to diluent is about 1:4 to about 1:0.1.
18. The method of claim 16 where the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5.
19. The method of claim 16 where the composition has a viscosity of from about 0.8 to about 15 centipoise.

The following claims (claim 20, 21, 22, 23, and 24) are derived from the original claim 14 . The term “or sedative effect” in claims 50 and 51 derives from page 7 : “formulations of phospholipid coated microdroplets of propofol devoid of fats and triglycerides that provide anesthesia and chronic sedation ...”

20. [The] A method of inducing anesthesia or sedation comprising administering to a subject in need of same an [anesthetic]anesthesia- or sedation-inducing amount of a stable, sterile, and antimicrobial injectable aqueous dispersion of a water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of about 1% to about 15% of propofol as the active ingredient, up to about 7% of a propofol soluble diluent, and about 0.8% to about 4% of a surface stabilizing amphiphilic agent, and the aqueous phase comprising a pharmaceutically acceptable water-soluble polyhydroxy tonicity modifier, the composition being devoid of additional bactericidal or bacteriostatic preservative agents, provided the ratio of propofol to diluent is about 1:4 to about 1:0.1 and the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5, and the composition has a viscosity of from about 0.8 to about 15 centipoise.

21. [The] A method of inducing anesthesia or sedation comprising administering to a subject in need of same an [anesthetic]anesthesia- or sedation-inducing amount of a stable, sterile, and antimicrobial injectable aqueous dispersion of a water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of about 1% to about 15% of propofol as the active ingredient, up to about 7% of a propofol soluble diluent, and about 0.8% to about 4% of a surface stabilizing amphiphilic agent, and the aqueous phase comprising a pharmaceutically acceptable water-soluble polyhydroxy tonicity modifier, the composition being devoid of additional bactericidal or bacteriostatic preservative agents.
22. The method of claim 21 wherein the ratio of propofol to diluent is about 1:4 to about 1:0.1.
23. The method of claim 21 wherein the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5.
24. The method of claim 21 wherein the composition has a viscosity of from about 0.8 to about 15 centipoise.

The following claims (claim 25 to 30) are derived from dependent claims related to claim 15, above.

25. The method of any of claims 15, 16, 20, and 21 where the propofol-soluble diluent is one or more selected from isopropyl myristate, cholesteryl oleate, ethyl oleate, squalene, squalane, alpha-tocopherol, and Miglyol-810.
26. The method of any of claims 15, 16, 20, and 21 where the propofol-soluble diluent is one or more selected from pharmaceutically acceptable natural triglycerides from vegetable or animal sources,

pharmaceutically acceptable vegetable oils, and omega-3 polyunsaturated fish oils.

27. The method of any of claims 15, 16, 20, and 21 where the surface stabilizing amphiphilic agent is Lipoid E80, or Lipoid EPC, or Lipoid SPC, or Lipoid SPC-3, or phospholipon-90H or phospholipon-100H.
28. The method of any of claims 15, 16, 20, and 21 where the surface stabilizing amphiphilic agent is 1,2-dimristoyl-sn-glycero-3-phosphocholine, or 1,2-dimristoyl-sn-glycero-3-[phospho-rac-(1-glycerol)], or egg lecithin, or egg phosphatidylcholine, or soy phosphatidylcholine, or saturated soy phosphatidylcholine, or soy lecithin, or dimyristoylphosphatidylcholine, or dimyristoylphosphatidylglycerol.
29. The method of any of claims 15, 16, 20, and 21 where the tonicity modifier is sucrose, dextrose, trehalose, mannitol, lactose, or glycerol.
30. The method of any of claims 15, 16, 20, and 21 where the dispersion is suitable for intravenous injection.